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Inner Ear Abnormalities in Kabuki Make-Up Syndrome: Report of Three Cases

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Three patients, a female and two males, 28, 15, and 14 years of age, with Kabuki make-up syndrome (KMS) were studied for middle and inner ear abnormalities by using CT scanning of the petrous bones. All three patients had bilateral dysplasia of the inner ear, i.e., hypodysplasia of the cochlea, vestibule, and semicircular canals (so-called Mondini dysplasia), whereas their middle ears had no abnormalities. Audiometry demonstrated a sharp decrease in hearing of the high tone range, bilateral in one and unilateral in another, while the third patient was noncooperative. In view of these findings, it would be advisable to study each individual with KMS and hearing impairment for possible inner ear abnormalities. Am. J. Med. Genet. 92:87–89, 2000.

KEY WORDS: Kabuki make-up syndrome; Niikawa-Kuroki syndrome; Mondini dysplasia; hearing impairment

INTRODUCTION

Kabuki make-up syndrome (KMS), first described in 1981 [Niikawa et al., 1981; Kuroki et al., 1981], is a multiple congenital anomalies/mental retardation (MCA/MR) syndrome characterized by a peculiar face, mental retardation, postnatal growth deficiency, dermatoglyphic abnormalities, and skeletal anomalies [Niikawa et al., 1988]. More than 70 Japanese individuals [Tsukahara et al., 1997] and more than 100 non-Japanese individuals [Wilson, 1998] with the syndrome have been reported. Hearing impairment is frequent in KMS patients, accounting for 24% in a study of 62 patients [Niikawa et al., 1988], but we are aware of only one report of inner ear abnormalities in the syndrome [Toutain et al., 1997]. Here we describe three patients with such abnormalities.

SUBJECTS AND METHODS

Three patients with KMS are described: a 28-year-old female (patient 1), a 15-year-old male (patient 2), and a 14-year-old male (patient 3). Patient 1 had previously been reported by Niikawa et al. [1981; patient 1], and patients 2 and 3 have been described by Niikawa et al. [1988; cases 30 and 26]. Each patient had all the five cardinal manifestations of the syndrome, i.e., a peculiar face characterized by long palpebral fissures with ectropion of the lateral third of the lower eyelids, mental retardation, short stature, dermatoglyphic abnormalities, and skeletal anomalies (Fig. 1). None of the three patients had otitis media (Table I). Patient 1 had frequent otitis media and a conductive hearing loss revealed by audiography in her early childhood. However, she did not have any symptoms or findings of recurrent otitis media, otitis media exdertive, or otitis media chronica at age 25 years. Patient 1 had paralysis of the soft palate with a high-arched palate (Table I). Patients 2 and 3 had cleft of the soft palate surgically repaired at ages of 18 months and 26 months, respectively (Table I).

We performed computerized tomography (CT) of the petrous bones by using a GE 9800 unit and standard bone algorithms, sliced at 1.5 mm thickness in the axial and coronal planes. The following areas were studied: 1) the cartilaginous and bony portions of the external auditory canal; 2) the cavity and ossicles of the middle ear; and (3) the cochlea, vestibule, canals, and internal auditory meatus of the inner ear. Standard audiometric test [ANSI, 1978]was performed in patients 1 and 2, while patient 3 refused to participate in the test.

RESULTS

The CT studies showed, in all three patients examined, Mondini dysplasia of bilateral inner ears. The cochleas were flattened with only one or one-half turns, the vestibules were dilated, and the semicircular canals were deformed (Table I, Fig. 2). The external auditory canals and middle ears showed no abnormalities. Audiograms of patients 1 and 2 are shown in Figures 3 and 4, respectively. Sensorineural high tone

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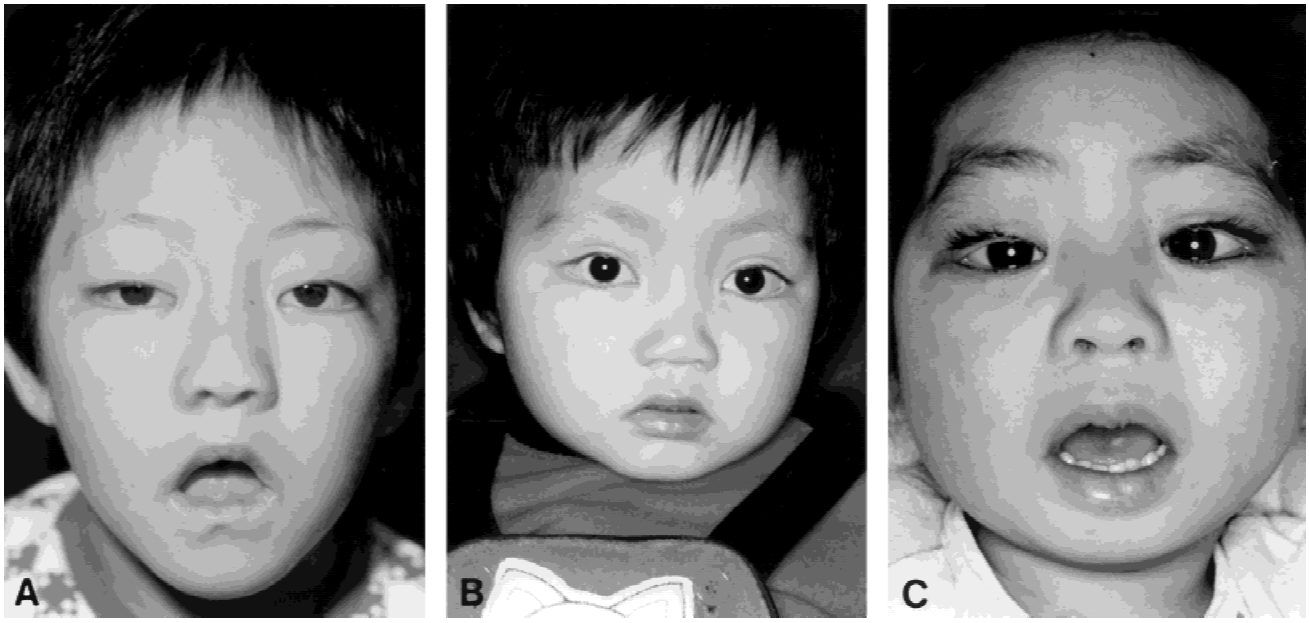

Fig. 1. Patients 1 (**A**), 2 (**B**), and 3 (**C**) at ages 6, 2, and 2 years, showing the facial appearance typical for Kabuki make-up syndrome.

loss of hearing over 2,000 Hz was found bilaterally in patient 2 and in the right ear of patient 1. Patient 3 refused to participate in audiometry. Since he was able to communicate by phonetical language, severe bilateral hearing disability could be ruled out, but uni- or bi-lateral high tone loss could not be excluded.

DISCUSSION

Niikawa et al. [1988], in their review of 62 patients with KMS, reported recurrent otitis media in 55% and hearing loss in 24% of the patients reviewed. The hearing loss has usually been attributed to otitis media, although several cases have been described with sensorineural [Kuroki et al., 1981; Burke and Jones, 1995] or mixed hearing loss [Carcione et al., 1991; Philip et al., 1992; Burke and Jones, 1995]. In the present study, all three patients studied had Mondini dysplasia of bilateral inner ears. Sensorineural hearing loss of over 2,000 Hz was observed in two of the two patients examined, unilateral in one, and bilateral in the other. These findings indicate inner ear abnormalities as a mechanism causing hearing impairment in KMS.

Mondini dysplasia involves anomalies of osseous and membranous labyrinths, both of which develop during the 6th to 9th weeks of embryonal life [Paparella, 1980; Schuknecht, 1980]. The dysplasia is characterized by a short and flat cochlea with only 1 to 1.5 turns instead of the usual 2.5 to 2.75, large vestibule, wide, small, or missing semicircular canals, bulbous endolympathic duct and sac, and immature sensorineural structures. It is the most common malformation of the inner ear [Carey, 1993]. The auditory function of the individuals with the syndrome may range from marked deafness to partial loss of hearing because it exhibits a wide spectrum of structural and functional abnormalities of the inner ear. The degree of hearing loss in the dysplasia depends on the extent of the changes in stria vascularis, organ of Corti, spiral ganglion, and other parts of the cochlear system. Therefore, sensorineural hearing impairment with high tone loss in our patients with KMS may be attributable to Mondini dysplasia of the inner ear.

Toutain et al. [1997] reported a 7-year-old girl with KMS and severe bilateral deafness due to Mondini dysplasia of the inner ear. Therefore, it is advisable to perform in early infancy CT scanning of the petrous bones and audiometry in each individual with KMS. Early detection of the inner ear abnormalities would lead to early preventive management of resulting complications and the use of hearing aids.

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TABLE I. Ear and Oral Findings of the Three Patients With Kabuki Make-Up Syndrome

	Patient number		
	1	2	3
High tone loss on audiometric finding	Right	Bilateral	
Inner ear abnormality	Mondini dysplasia bilateral	Mondini dysplasia bilateral	Mondini dysplasia bilateral
Middle ear abnormality	—	—	—
External ear abnormality	—	—	—
Otitis media	—	—	—
Palatal abnormality of soft palate	Palalysis	Cleft soft palate (repaired)	Cleft soft palate (repaired)

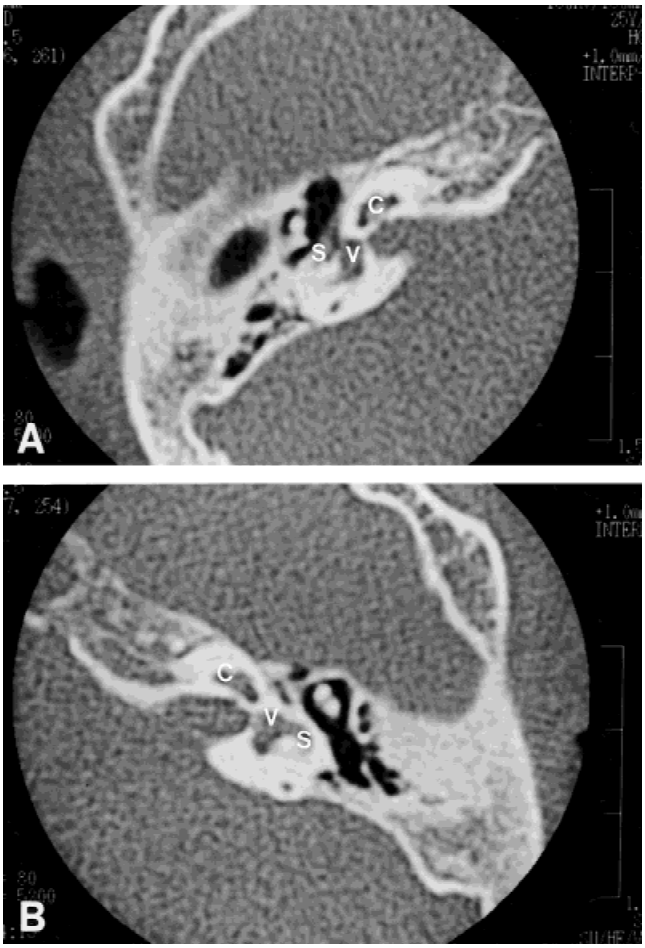

Fig. 2. CT of the right (**A**) and left (**B**) inner ears of patient 1, showing bilateral Mondini dysplasia: flattened cochleas with only one-half turns (C), saccular dilatation of the vestibules (V), and deformed horizontal semicircular canals (S).

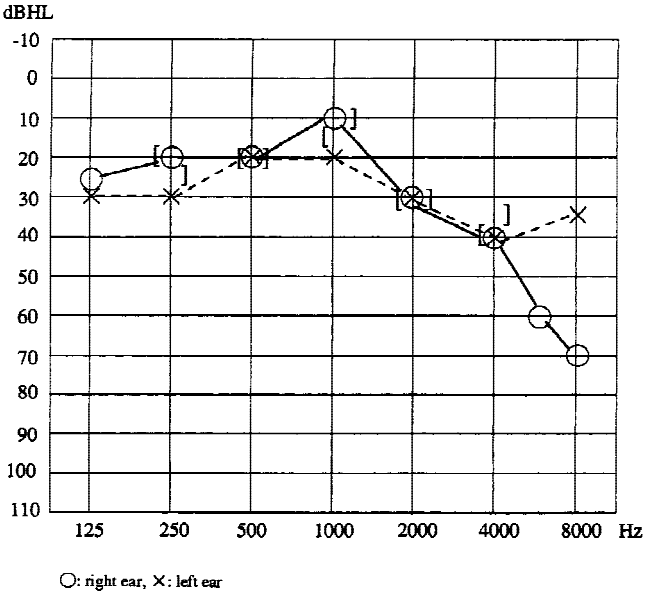

Fig. 3. Audiogram of patient 1, showing a sharp decrease of hearing in the high frequency area (>2,000 Hz) in the right ear.

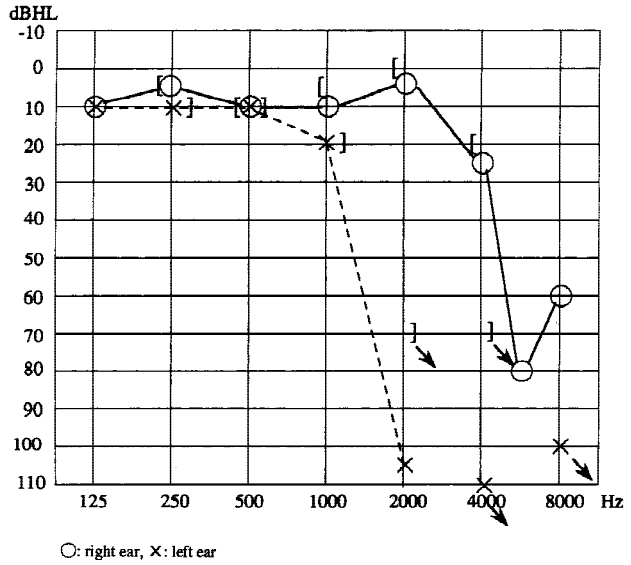

Fig. 4. Audiogram of patient 2, showing a sharp decrease of hearing in the high frequency area (>2,000 Hz) in both ears.

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